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(54) Title: COMPOSITIONS, SPLICE VARIANTS AND METHODS RELATING TO BREAST SPECIFIC GENES AND PROTEINS

(57) Abstract: The present invention relates to newly identified nucleic acid molecules and polypeptides present in normal and neoplastic breast cells, including fragments, variants and derivatives of the nucleic acids and polypeptides. The present invention also relates to antibodies to the polypeptides of the invention, as well as agonists and antagonists of the polypeptides of the invention. The invention also relates to compositions containing the nucleic acid molecules, polypeptides, antibodies, agonists and antagonists of the invention and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating breast cancer and non-cancerous disease states in breast, identifying breast tissue, monitoring and identifying and/or designing agonists and antagonists of polypeptides of the invention. The uses also include gene therapy, production of transgenic animals and cells, and production of engineered breast tissue for treatment and research.



WO 2004/053077 A3

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/38815

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 21/04, 21/02; C12Q 1/68, C12P 21/06; C12N 1/20; 15/00, 5/00; A01N 63/00; A61K 39/02  
 US CL. : 536/23.5, 23.1, 24.3; 435/6, 69.1, 252.3, 320.1, 325; 424/93.2, 200.1

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.5, 23.1, 24.3; 435/6, 69.1, 252.3, 320.1, 325; 424/93.2, 200.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category *    | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No.    |
|---------------|--|--------------------------|
| X<br>---<br>A | RAMALHO, J.S. et al. Chromosomal mapping, gene structure and characterization of the human and murine RAB27B gene. BMC Genetics. February 2001, Vol. 2, No. 2, 13 pages, see especially the reference to GenBank Accession No. AF329499 on the last page.  | 1-6, 8-10<br>-----<br>7  |
| X<br>---<br>A | Database NCBI, RAMALHO, J.S. et al. 'Homo sapiens RAS-related protein RAB27B mRNA, complete cds'. GenBank [online]. July 2002 [retrieved on 2004-07-15]. Retrieved from the Internet:<br><URL: <a href="http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=nucleotide&amp;val=12963390">http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=nucleotide&amp;val=12963390</a> >. GenBank Accession No. AF329499 nucleotides 482-711 are identical to nucleotides 414-643 of Applicants' SEQ ID No. 1. | 1, 4, 5, 6<br>-----<br>7 |
| X<br>---<br>A | US 2002/0115057 A1 (YOUNG) 22 August 2002 (22.08.2002), pages 1-14, especially page 1; page 4 [0052]; page 10 [0108]; page 12 Sequence Listing section; and nucleotides 331-560 of SEQ ID No. 563 which are identical to nucleotides 414-643 of Applicants SEQ ID No. 1.   | 1-6, 8-10<br>-----<br>7  |
| X<br>---<br>A | WO 01/34643 A1 (HUMAN GENOME SCIENCES, INC.) 17 May 2001 (17.05.2001), pages 1-4 and 150-154 of the description, and page 37 of the sequence listing. Nucleotides 423-1103 of SEQ ID No. 59 on page 37 are identical to nucleotides 829-1509 of Applicants SEQ ID No. 49.  | 1-6, 8-10<br>-----<br>7  |



Further documents are listed in the continuation of Box C.



See patent family annex.

| * Special categories of cited documents:  |  |
|---|--|
| "A" document defining the general state of the art which is not considered to be of particular relevance  | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "B" earlier application or patent published on or after the international filing date   | "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "O" document referring to an oral disclosure, use, exhibition or other means  | "&" document member of the same patent family  |
| "P" document published prior to the international filing date but later than the priority date claimed  |  |

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# INTERNATIONAL SEARCH REPORT

PCT/US03/38815

## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category *    | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No.   |
|---------------|---|-------------------------|
| X<br>---<br>A | WO 00/58473 A2 (CURAGEN CORPORATION) 5 October 2000 (05.10.00), pages 1-5, 38-42, 59-63 and 4793-4794 . Nucleotides 184-911 of SEQ ID No. 5611 on pages 4793-4794 are identical to nucleotides 354-1078 of Applicants' SEQ ID No. 50. | 1-6, 8-10<br>-----<br>7 |

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/38815

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: Groups 1, 49 and 50 (drawn to Claims 1-10 and SEQ ID Nos. 1, 49 and 50)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

PCT/US03/38815

### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1 (Claims 1-10) drawn to an isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID No. 1,...Group 232 (Claims 1-10) drawn to an isolated nucleic acid molecule comprising the nucleic acid sequence that encodes the amino acid sequence of SEQ ID No. 232, where each group is drawn to a single nucleic acid molecule sequence of SEQ ID Nos. 1-95 or a single amino acid sequence of SEQ ID Nos. 96-232.

Group 233 (Claims 11 and 12) drawn to a polypeptide encoded by the nucleic acid molecule sequence of SEQ ID No. 1,...Group 464 (Claims 11 and 12) drawn to a polypeptide encoded by the nucleic acid sequence that encodes the amino acid sequence of SEQ ID No. 232, where each group is drawn to a single nucleic acid molecule sequence of SEQ ID Nos. 1-95 or a single amino acid sequence of SEQ ID Nos. 96-232.

Group 465 (Claim 13) drawn to an antibody or fragment thereof that binds to a polypeptide encoded by a nucleic acid molecule sequence of SEQ ID No. 1,...Group 696 (Claim 13) drawn to an antibody or fragment thereof that binds to a polypeptide comprising the amino acid sequence of SEQ ID No. 232, where each group is drawn to a single nucleic acid molecule sequence of SEQ ID Nos. 1-95 or a single amino acid sequence of SEQ ID Nos. 96-232.

Group 697 (Claim 14) drawn to a method for determining the presence of a breast specific protein comprising an amino acid sequence with at least 95% identity to SEQ ID No. 96,...Group 833 (Claim 14) drawn to a method for determining the presence of a breast specific protein comprising an amino acid sequence with at least 95% identity to SEQ ID No. 232, where each group is drawn to a single amino acid sequence of SEQ ID Nos. 96-232.

Group 834 (Claim 15) drawn to a method for diagnosing or monitoring the presence and metastases of breast cancer in a patient comprising determining the amount of an isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID No. 1 or a polypeptide encoded thereby,...Group 1065 (Claim 15) drawn to a method for diagnosing or monitoring the presence and metastases of breast cancer in a patient comprising determining the amount of an isolated nucleic acid molecule comprising the amino acid sequence of SEQ ID No. 232 or a polypeptide encoded thereby, where each group is drawn to a single nucleic acid molecule sequence of SEQ ID Nos. 1-95 or a single amino acid sequence of SEQ ID Nos. 96-232.

Group 1066 (Claim 16) drawn to a kit for detecting a risk/presence of cancer in a patient comprising a means for determining the presence of an isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID No. 1 or a polypeptide encoded thereby,...Group 1297 (Claim 16) drawn to a kit for detecting a risk/presence of cancer in a patient comprising a means for determining the presence of an isolated nucleic acid molecule comprising the amino acid sequence of SEQ ID No. 232 or a polypeptide encoded thereby, where each group is drawn to a single nucleic acid molecule sequence of SEQ ID Nos. 1-95 or a single amino acid sequence of SEQ ID Nos. 96-232.

Group 1298 (Claim 17) drawn to a method of treating a patient with breast cancer comprising administering a composition consisting of an isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID No. 1 or a polypeptide encoded thereby,...Group 1529 (Claim 17) drawn to a method of treating a patient with breast cancer comprising administering a composition consisting of an isolated nucleic acid molecule comprising the amino acid sequence of SEQ ID No. 232 or a polypeptide encoded thereby, where each group is drawn to a single nucleic acid molecule sequence of SEQ ID Nos. 1-95 or a single amino acid sequence of SEQ ID Nos. 96-232.

Group 1530 (Claim 18) drawn to a vaccine comprising a nucleic acid molecule sequence of SEQ ID No. 1,...Group 1761 (Claim 18) drawn to a vaccine comprising a polypeptide comprising the amino acid sequence of SEQ ID No. 232, where each group is drawn to a single nucleic acid molecule sequence of SEQ ID Nos. 1-95 or a single amino acid sequence of SEQ ID Nos. 96-232.

## INTERNATIONAL SEARCH REPORT

PCT/US03/38815

The inventions listed as Groups 1-1761 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group 1 is the isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID No. 1. The claims included in Group 1 (Claims 1-10) are claims to the isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID No. 1, claims to products comprising the isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID No. 1, and claims to a first appearing method of using the isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID No. 1.

Groups 1-232 do not share a special technical feature because they are each drawn to different chemical compounds (isolated nucleic acid molecules comprising the nucleic acid sequences of SEQ ID Nos. 1-95 or isolated nucleic acid molecules encoding the amino acid sequences of SEQ ID Nos. 96-232) having no special technical feature in common. The same is true of Groups 233-464, 465-696, 697-833, 834-1065, 1066-1297, 1298-1529 and 1530-1761.

Groups 1-232, 233-464, 465-696, 697-833, 834-1065, 1066-1297, 1298-1529 and 1530-1761 are drawn to different nucleic acid/polypeptide molecules, different methods of using those molecules and/or different products relating to those molecules. The nucleic acid/polypeptide molecules differ from each other because they are different chemical compounds having no special technical feature in common, as mentioned above. The methods using those products are different because they comprise different method steps. The products relating to those molecules are completely different products. Furthermore, the nucleic acid/polypeptide molecules and the products relating to those molecules are not limited to being used for only the claimed methods, and can be used for other methods. Therefore, Groups 1-1761 are not so linked by a special technical feature within the meaning of PCT Rule 13.2 as to form a single general inventive concept.

### Continuation of B. FIELDS SEARCHED Item 3:

USPTO STIC-Biotech library conducted search of the following databases: Published\_Applications\_NA; Issued\_Patents\_NA; GenEmbl; N\_Genseq; and EST